Defining "Value" in Translation of Genomic-Based Research

IOM Roundtable
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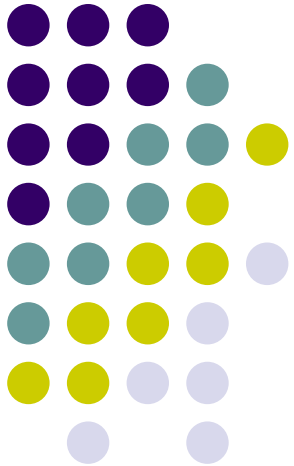
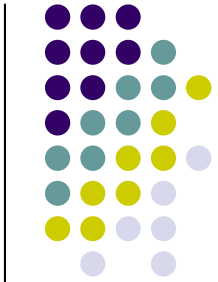


Outline

- What is ‘value’ in genomic-based translational research, specifically pharmacogenomics (PGx)?
- How to measure economic value in PGx?
- Challenges to assessing value and implications for translation of PGx technologies

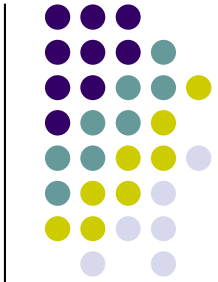
New Importance of Value of PGx



- Implications of broader availability of PGx testing for commonly used drugs
- FDA guidance to maximise the translation of PGx from ‘bench to bedside’
  - Requirements for submission of PGx data alone and in combination
  - Critical Path Initiative to address the ‘pipeline problem’
- Concerns about adverse drug reactions and increasing prescription costs

-FDA Guidance for industry: pharmacogenomic data submissions, 2005
-Lesko, Report of the DrugSafe Workshop, 2003

Value is New Buzzword

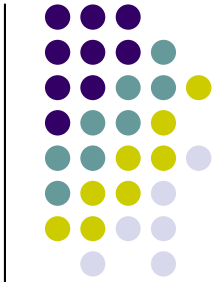


- "How much will the expanded use of genetic information further escalate the cost of healthcare, and who will pay for it?

  - Harold Varmus, MD, former Director of NIH. NEJM 2002; 347:1526-7

- In past decade, there has been:
  - 80% growth in number of new drugs prescribed
  - 100% growth in new device patents
  - 1,500% growth in diseases with gene tests

What is 'Value' in Genomic-Based Translational Research?



- For successful adoption into clinical practice, a PGx test has to demonstrate:
  - Analytic validity – accuracy of test for genotype
  - Clinical validity – accuracy for clinical outcome
  - Clinical utility – ability to inform clinical decision making, prevent adverse outcomes, predict outcomes
  - Economic value - impact on health sector, cost-effectiveness, and commercial viability

- Secretary's Advisory Committee on Genetics, Health and Society, 2007

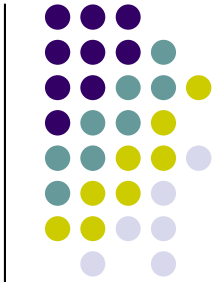
Outline

- What is ‘value’ in genomic-based translational research, specifically pharmacogenomics (PGx)?

- **How to measure economic value in PGx?**
  - Evaluating cost-of-illness
  - Criteria for cost-effectiveness of PGx
  - Criteria for PGx to be economically viable in the marketplace

- Challenges to assessing value and implications for translation of PGx technologies

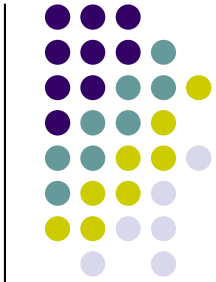
How to Measure Economic Value of PGx?



1) Cost-of-Illness	Value from population perspective. Examine size of the problem in monetary terms. What is the relevant population and cost of disease burden?
2) Cost-effectiveness	Value within the relevant population. Examine efficiency measured as marginal cost per unit of effectiveness from PGx versus standard care.
3) Market economics	To what extent is value-based pricing possible? What is a fully informed patient willing-to-pay for PGx? Examine societal net-benefit.

-Phillips K. Nature Reviews 2005;4:499-509
-Garrison L. Drug Information Journal 2007;41:501-9

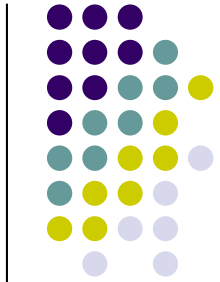
1) Data for Cost-of-Illness of PGx



Relevant Data	Description	Example HER2 and Trastuzumab
Prevalence of condition for drug treatment	Size of the population for testing	Prevalence of patients with metastatic BC
Mutation prevalence	Size of the population in which testing could impact outcome	20-30% of BC patients overexpress HER-2
Utilization	Extent to which testing will be undertaken	Test costs $100 to $400
Drug Expenditures	Testing could change drug utilization	Annual cost of treatment ~$30 to $80K
Condition expenditures	Measure clinical outcomes of testing on condition	25% increase in median survival

- *Adapted from Phillips K. Nature Reviews 2005;4:499-509*

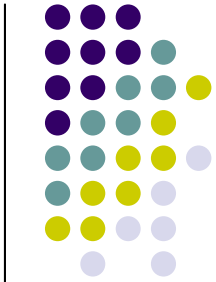
2) Cost-Effectiveness



$$\text{Incremental Cost-Effectiveness} = \frac{\Delta \text{ Cost}}{\Delta \text{ Effect}}$$

$$= \frac{\text{Cost (A)} - \text{Cost (B)}}{\text{Effect (A)} - \text{Effect (B)}}$$

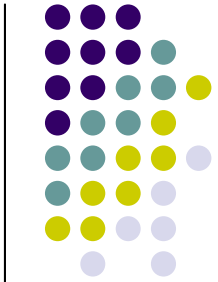
Criteria for Cost-Effectiveness of PGx



Factors	Characteristics Favouring Cost-Effectiveness
Prevalence of mutation	Variant allele frequency is relatively high
Severity of Disease and Outcomes Avoided	Severe outcome, high mortality, significant impact on quality of life, or expensive medical care costs
Drug Monitoring	Monitoring of drug response currently not practiced or difficult
Gene and Outcome Association	Strong association between gene variant and clinically relevant outcomes
Test performance and cost	A rapid and relatively inexpensive, but accurate test is available

-*Veenstra D et al, Pharmaceutical Sci, Sept 2000.*
-*Phillips K et al. Am J Managed Care 2004;10:425-32*

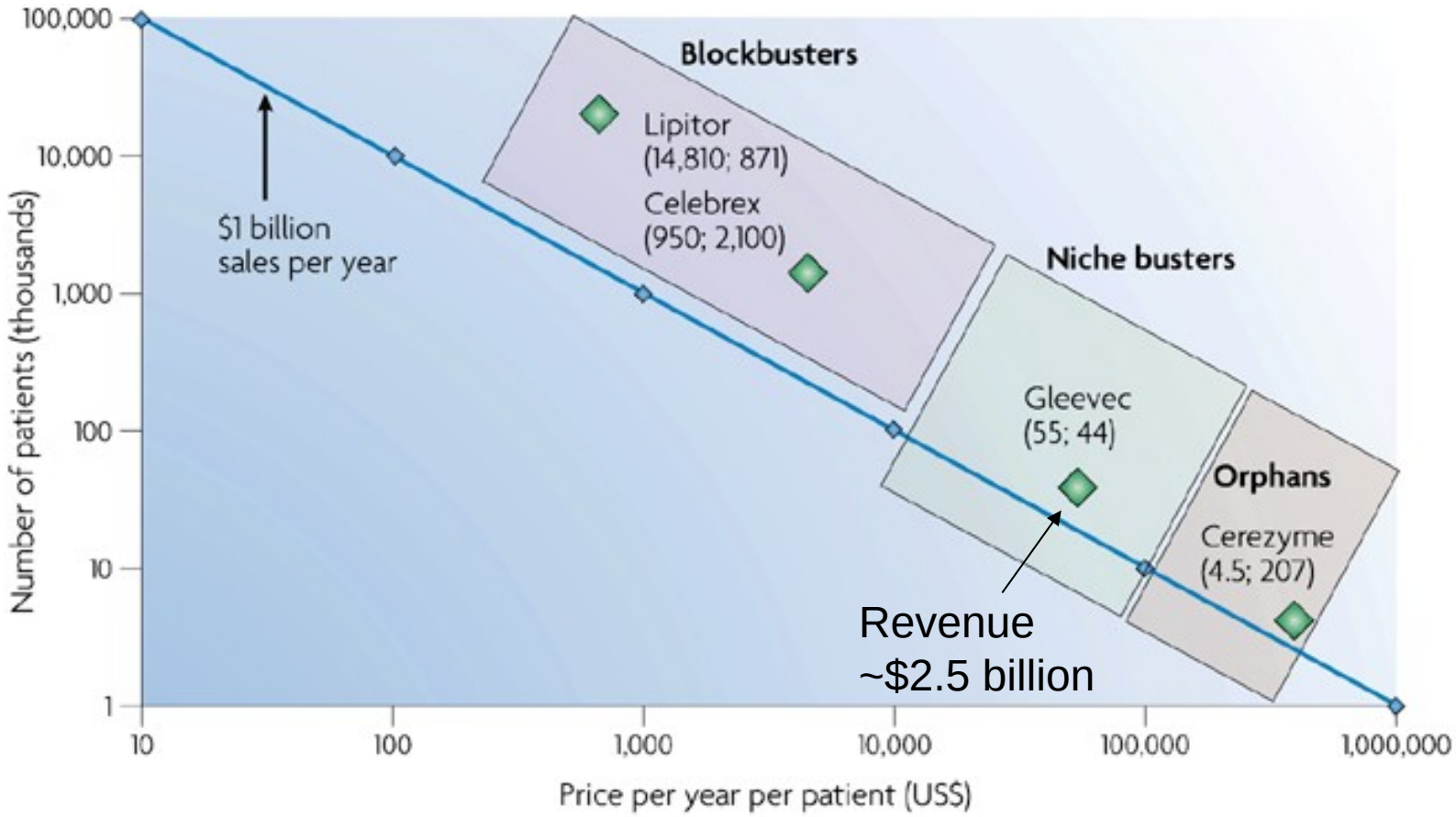
3) Criteria for Market Economics: Value-Based Pricing



- Ability of diagnostic test to identify appropriate patient subpopulation and treatment to demonstrate improved response
- Value-based flexible pricing for both the test and drug will provide stronger incentive for innovation
- Test manufacturer needs intellectual property protection
- Additional regulatory market protection

- *Trusheim MR et al. Nature Reviews March 2007;1-7*
- *Garrison L. Drug Information Journal 2007;41:501-9*

Large Revenues are Possible: Higher Pricing in Target Population for Higher Efficacy



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Outline

- What is ‘value’ in genomic-based translational research (specifically pharmacogenomics (PGx)?
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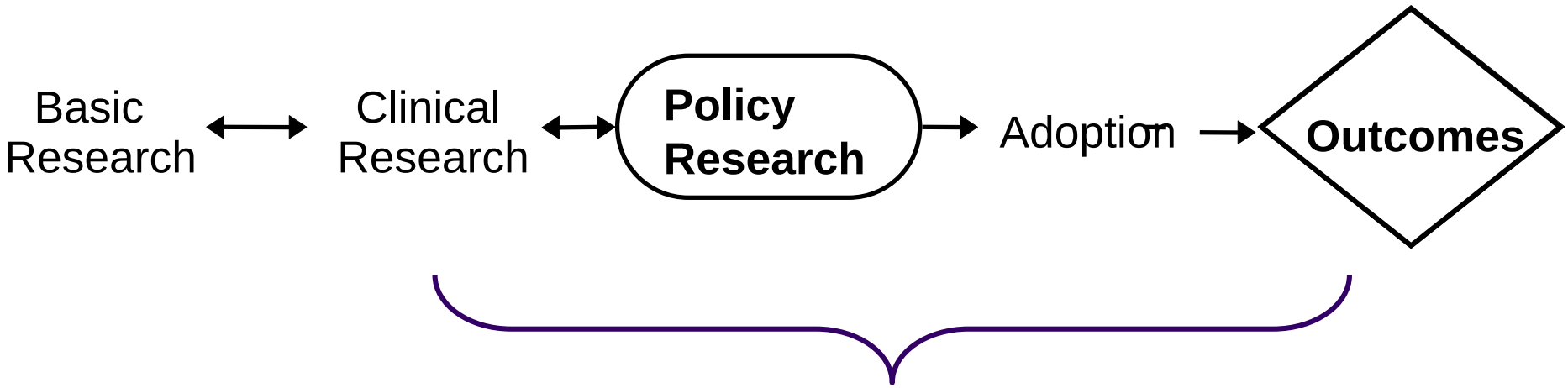
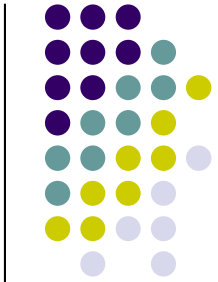
Translational Research Continuum Requires:



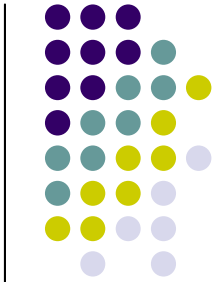
PGx must fill a knowledge gap that is clinically important to the diagnosis, prognosis and treatment of patients

1) Lack of Data and Evidence of Effectiveness



- Lack of data on utilization and outcomes or comprehensive databases
- Debate on whether observational data provides sufficient evidence of clinical utility
  - but RCTs for all genetic tests is infeasible

Example of Lack of Data: HER-2/neu and Trastuzumab



- No secondary dataset available to examine utilization (!!??) so conducted chart review

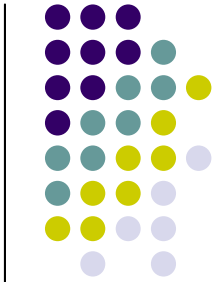
- Results (based on pilot only)
  - Wide variation in type of testing performed
    - Majority get one test (IHC), fewer get FISH, some get both
  - Variation in trastuzumab use by HER2/neu status
    - 56% of patients had documentation of clearly positive test

- Consistent w/ proprietary insurer study & anecdotal information
  - 10%-40% taking trastuzumab do not have clearly positive test
  - 20% of tests are inaccurate

2) Few Economic Models for PGx

- Must demonstrate value for adoption and reimbursement
- Few economic analyses of PGx
  - Diagnostics have historically been less studied than drugs
  - Up-front testing costs perceived to be higher than downstream savings
  - Value of prevention harder to measure
- Many (most?) products are not evaluated early enough!!!
  - Analyses done after intervention becomes widely accepted are not as useful

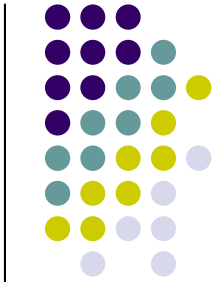
3) Need to Model Complex Clinical Pathways



- Particularly an issue with a test/treatment combination
- Many models have not adequately considered testing variability (sensitivity and specificity, sequencing, timing)

- Example: HER-2 testing for trastuzumab
  - Most analyses have assumed “perfect” testing
  - But test inaccuracy, variation testing performance and women getting treatment without evidence of a positive test

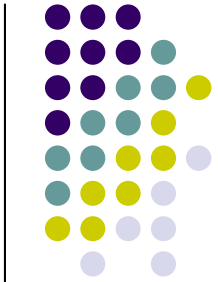
4) May Need to Consider Multiple Populations



- Models often don't examine systematic differences between patient sub-groups

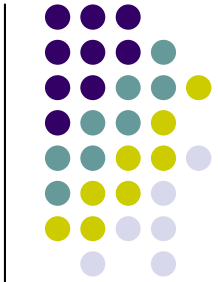
- Example: Lynch syndrome screening (HNPCC)
  - Individuals with syndromes have ~80% chance of colorectal cancer
  - Testing involves both probands (individuals with cancer) and relatives – very different situations

5) Need to Build Evidence Base for PGx



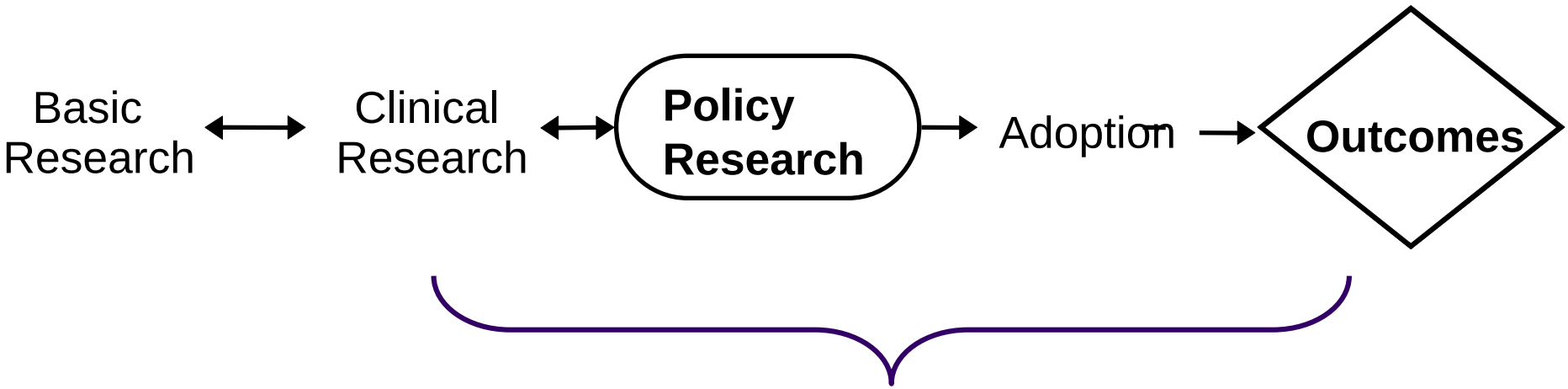
- Lack of evidence about gene-based applications -far more studies of genetic associations than studies on what to do with the information
- Need evidence on:
  - Analytic & clinical validity of test
  - Clinical utility of testing & intervention
  - Test availability and utilization
  - Impact on health and economic outcomes
  - Health burden

One Approach to Building Evidence Base



- Evaluation of Genomic Applications in Practice and Prevention Working Group (EGAPP)
- Model project initiated in fall 2004 by CDC
- Goal: develop coordinated process for evaluating translation of genomic applications
- Initial recommendations included:
  - CYP450 testing for SSRIs
  - HNPCC (Lynch syndrome) screening (colorectal cancer)
  - UGT1A1 testing for colorectal cancer tx (irinotecan)
  - Gene expression profiling for breast cancer (Oncotype, Mammaprint)

Translational Research Continuum Requires:



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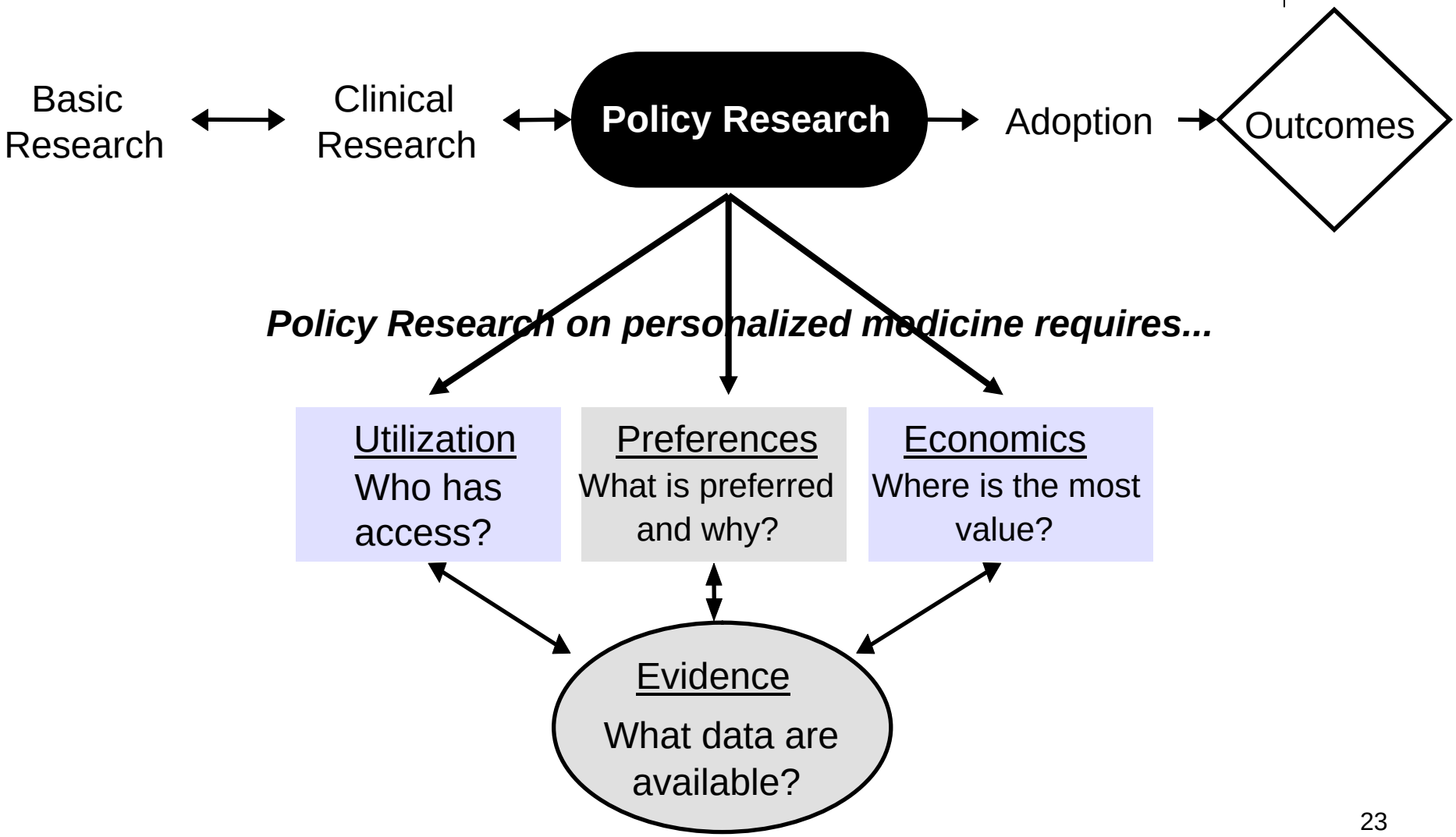
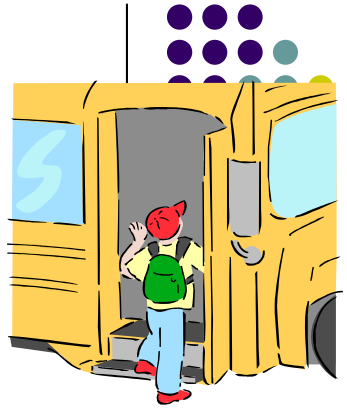
Cancer & Personalized Medicine Research Study (CANPERS)

Objective: Use integrated, interdisciplinary approach to obtain evidence about key aspects of translation of genomic information for breast and colorectal cancer into clinical practice and health policy.

CANPERS Conceptual Framework



“The Train has Left the Station”



- PGx is an inevitable trend for the future
- A key aspect is demonstrating value using economic analyses
- There are multiple challenges and building the evidence base that captures the health burden, utilization, clinical utility cost-effectiveness etc of PGx will be critical

Thank you!